

PESTICIDES

Applied pesticide toxicity shifts toward plants and invertebrates, even in GM crops

Ralf Schulz^{1,2*}, Sascha Bub¹, Lara L. Petschick¹, Sebastian Stehle^{1,2}, Jakob Wolfram¹

Pesticide impacts are usually discussed in the context of applied amounts while disregarding the large but environmentally relevant variations in substance-specific toxicity. Here, we systemically interpret changes in the use of 381 pesticides over 25 years by considering 1591 substance-specific acute toxicity threshold values for eight nontarget species groups. We find that the toxicity of applied insecticides to aquatic invertebrates and pollinators has increased considerably—in sharp contrast to the applied amount—and that this increase has been driven by highly toxic pyrethroids and neonicotinoids, respectively. We also report increasing applied toxicity to aquatic invertebrates and pollinators in genetically modified (GM) corn and to terrestrial plants in herbicide-tolerant soybeans since approximately 2010. Our results challenge the claims of a decrease in the environmental impacts of pesticide use.

Recent debates about the potential side effects of pesticides on humans (1) and the environment (2, 3) have been dominated by the comparison of use rates (e.g., kilograms per hectare) or applied amounts (e.g., kilograms per year) (4–9). These weight-based measures are not necessarily informative from an environmental perspective because toxicity among pesticides varies over several orders of magnitude (tables S1 to S3). This suggests that environmental effects strongly depend on the shares of individual pesticides in the total applied amount (1).

In this study, we extended a weight-based assessment of 381 pesticides for the years 1992 to 2016 (figs. S1 to S3) by 1591 regulatory threshold levels (RTLs) [as officially derived thresholds indicative of potential biodiversity impacts (3)] for eight different groups of nontarget species (10). We multiplied the annually applied amount (i.e., mass) of individual pesticides [data from the US Geological Survey (USGS)] with the reciprocal of the pesticide- and species group-specific RTLs (10) [data mainly from the US Environmental Protection Agency (EPA), see tables S1 and S2; species groups were unequally represented, see table S5] to derive the total applied toxicity (TAT) per substance, species group, and year (for TAT sensitivity, see fig. S4). The TAT is predictive of the potential pesticide impact (fig. S5). The annual TAT values were aggregated over different sets of substances (e.g., pesticide use types, chemical classes, and modes of action) to derive relative measures of temporal trends in agriculture both overall and for genetically modified (GM)-dominated crops specifically.

A comparison of the applied pesticide amount and the TAT reveals different temporal phases

for the different species groups. Regarding vertebrate toxicity (Fig. 1A), great reductions in acute toxicity have been achieved over the past few decades, driven almost entirely by insecticides (fig. S6A), whose TATs decreased by approximately a factor of 9 for mammals (Fig. 1C) and birds (Fig. 1D) through the replacement of organophosphorus and carbamate insecticides by pyrethroids and neonicotinoids (figs. S2 and S7, A and B). This development, which coincided with a proportional decrease in the applied amount (Fig. 1A, phase a) and an increase in corn acreage (fig. S10A), occurred in response to the high toxicity found in vertebrates (9). The fish TAT (TAT_{fish}) (Fig. 1B) remained constant overall since 2004 because of pyrethroid toxicity, which is relevant for this group (fig. S7C).

In sharp contrast, the invertebrate TAT has markedly increased since approximately 2005 (Fig. 1E, phase c). Both aquatic invertebrate TAT ($TAT_{\text{aqua-inverts}}$) and $TAT_{\text{pollinators}}$ more than doubled, with an increase of ~8% per year between 2005 and 2015 (Fig. 1, F and G; fig. S6B; and fig. S8, A and C), whereas the terrestrial arthropod TAT ($TAT_{\text{terr-arthropods}}$) (referring here to nonpollinating species) increased less (Fig. 1H and figs. S6B and S8B; note, there is lower data availability for terrestrial arthropods, table S5). The TAT was driven solely by insecticides in all invertebrate groups (fig. S6B), coinciding with a proportional increase in cultivated area in relevant crops (figs. S10, B and C, and S11). Simultaneously, the applied insecticide amount decreased by ~40% (fig. S1B).

Although pollinators and aquatic invertebrates show similar temporal patterns regarding the applied amount of pesticides and TAT (Fig. 1E, phases b and c), the toxicities are driven by distinct classes of insecticides. For pollinators—e.g., bees or bumble bees—neonicotinoids are increasingly responsible for the TAT (Fig. 1G and fig. S8A). Neonicotinoids have been documented as being highly

toxic to bees (11, 12), and some of them have therefore been banned in the European Union (EU). Although seed treatments constitute >80% of all neonicotinoid use in the US (4) and restrictions on postbloom applications in perennial (tree) crops receiving spray applications have reduced pollinator risks (13), neonicotinoid use remains problematic (12), for example because of oral-based bee toxic load, which has increased particularly in heartland corn and soybeans (13). For aquatic invertebrates (e.g., crustaceans, mayflies, caddisflies, and dragonflies), pyrethroid insecticides have dominated the TAT since 1992, and they have also become increasingly relevant for terrestrial arthropods (nonpollinators such as mites, flies, and beetles; Fig. 1, F and H, and fig. S8, B and C). Figure 1E highlights a regime shift in the evolution of pesticide use in the mid-2000s (phase bc), when a phase of prevailing structural change in insecticide use (b) turned into a phase of TAT growth that is completely decoupled from trends in the total applied amount (c). Increases in applied pyrethroid toxicity have previously been implied only for fish (14). In the case of $TAT_{\text{aqua-inverts}}$, just four pyrethroids explained >80% of the increase since 2006. Because the detection limits of these four compounds in water are more than two orders of magnitude higher than their respective RTLs (table S3), it appears virtually impossible to track them at the entire range of ecologically relevant concentrations through scientific monitoring efforts (3, 15, 16). The highly effective, low-use rate insecticides (tables S3 and S4), often associated with an environmentally benign character (6, 9), increase in toxicity and use (fig. S12) and have the potential to be a considerable but widely unrecognized threat to both terrestrial and aquatic invertebrates (2, 3, 16).

The TAT for nontarget plants, which has been driven solely by herbicide use, showed an upward trend since approximately 2006 (Fig. 1I, phases a' and f, and figs. S6C and S9), likely related to resistance in crops (17). Although no single mode of action dominates plant toxicity, growth regulators (e.g., acetochlor) contribute mainly to the terrestrial and aquatic plant TAT, and amino acid synthesis inhibitors, such as the increasingly used glyphosate (fig. S3B) and cell membrane disruptors (e.g., oxyfluorfen), contribute to the $TAT_{\text{terr-plants}}$ (Fig. 1, J and K, and fig. S9). The increases in plant TAT may have major impacts on terrestrial food webs, for example through reduced plant seed production (18) or plant species decline (19), requiring a systemic evaluation of previously unrecognized aspects of pesticide use.

Toxicity-weighted use is the strongest predictor of the potential impact of a pesticide on the environment (20). Its application in the

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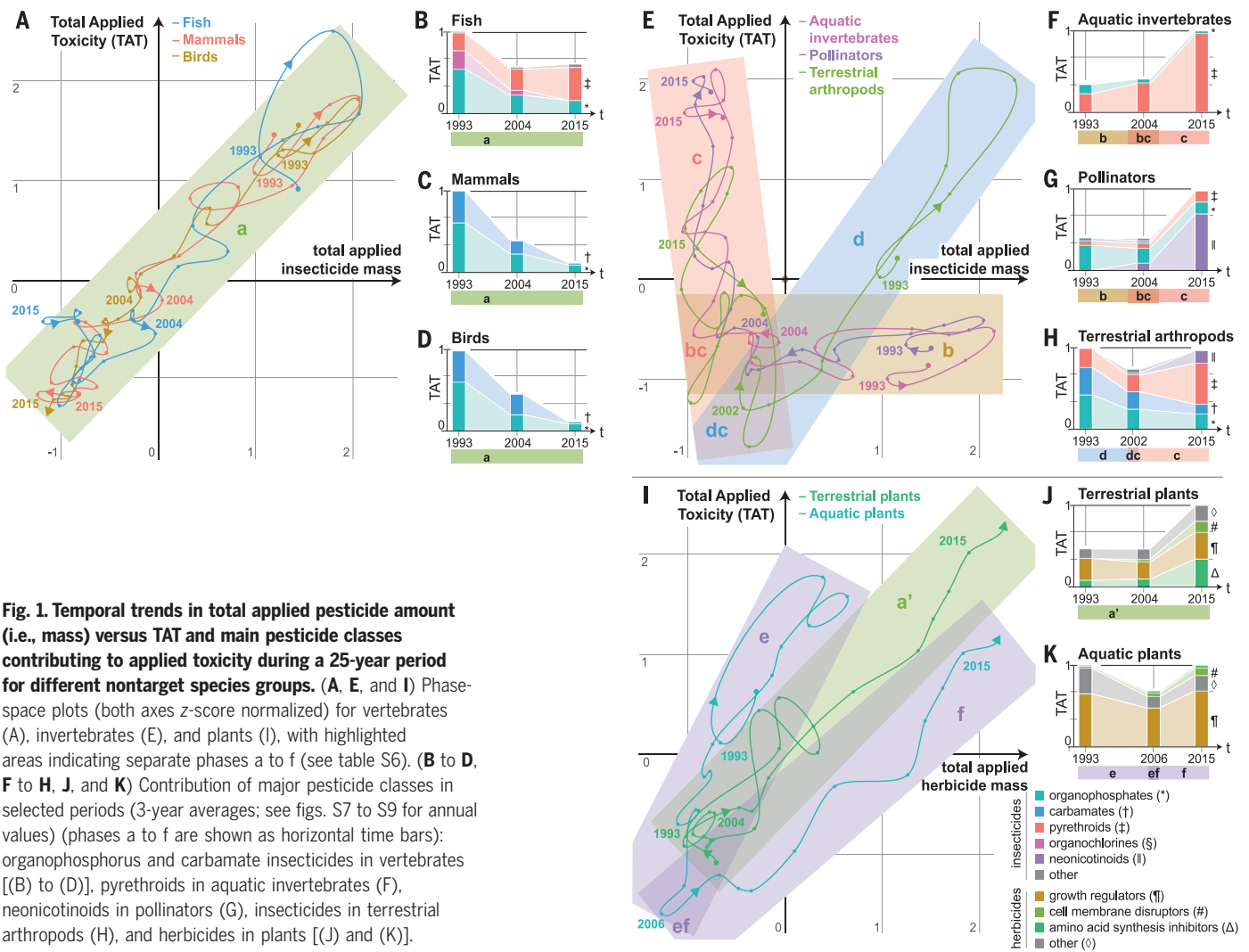


Fig. 1. Temporal trends in total applied pesticide amount (i.e., mass) versus TAT and main pesticide classes contributing to applied toxicity during a 25-year period for different nontarget species groups. (A, E, and I) Phase-space plots (both axes z-score normalized) for vertebrates (A), invertebrates (E), and plants (I), with highlighted areas indicating separate phases a to f (see table S6). (B to D, F to H, J, and K) Contribution of major pesticide classes in selected periods (3-year averages; see figs. S7 to S9 for annual values) (phases a to f are shown as horizontal time bars): organophosphorus and carbamate insecticides in vertebrates [(B) to (D)], pyrethroids in aquatic invertebrates (F), neonicotinoids in pollinators (G), insecticides in terrestrial arthropods (H), and herbicides in plants [(J) and (K)].

present study relies on the assumption that pesticide use and its effects on organisms are robustly connected to each other at large scales, even though there is tremendous variability in substance properties (table S4), application patterns, and local exposure situations. This assumption is, however, supported by multiple lines of evidence, even in the crucial case of pyrethroid risk to aquatic invertebrates. Monitoring data from a total of 89 available peer-reviewed studies [1977 insecticide concentrations from 231 different surface waters across the US (20, 21)] show that the rate at which measured insecticide and pyrethroid concentrations exceed the $RTL_{\text{aqua-inverts}}$ is significantly correlated with the applied toxicity to aquatic invertebrates (fig. S5). RTL exceedance in surface waters is indicative of negative effects on aquatic biodiversity (3), and pyrethroids exhibit the highest RTL exceedance rates (3, 21). Pyrethroids show adverse effects in midwestern streams (15), occur regularly in stream biofilms (22), and even cause resistance in nontarget freshwater am-

phipods (23). Taken together, multiple lines of evidence provide a clear link between the use of, exposure to, and effects of pyrethroid insecticides in aquatic systems. This link likely also applies to other pesticide and species groups, although further investigation in this field is needed.

From a broader perspective, decreases in vertebrate TAT were achieved at the cost of increased invertebrate TAT (Fig. 1, A and E). Additionally, ecologically linked pollinators and terrestrial plants (11, 24) are among those with the largest TAT increases (Fig. 1, E and I). The cumulative direct impact of modern insecticides on invertebrates and the indirect impact of herbicides on invertebrates through the food chain thus likely contribute to the currently debated decline in arthropods (2, 3, 5, 25–27). This decline may ultimately lead to indirect effects on vertebrate predators (2).

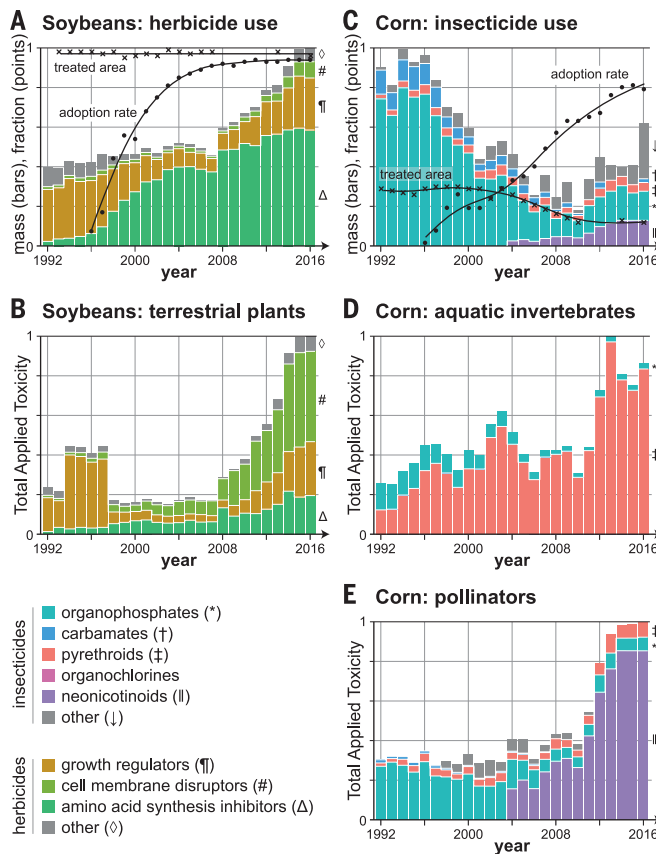
The TAT increased even in GM crops (Fig. 2, B, D, and F). Herbicide use has undergone substantial changes with the implementation of herbicide-tolerant GM crops (Fig. 2A),

which has led to a strong increase in the use of glyphosate (8, 28) (Fig. 2A and fig. S3B). $TAT_{\text{terr-plants}}$ has increased steadily since approximately 2008 for herbicides in herbicide-tolerant soybeans (Fig. 2B and fig. S14, A and B), likely in response to glyphosate resistance (17). However, downward trends have been reported for GM soybean herbicide toxicity to humans (1).

In the most widely grown GM crop that produces a *Bacillus thuringiensis* (*Bt*) toxin, corn, the insecticide TAT increased. Considering only data for corn, of which 79% in 2016 was *Bt* hybrids (Fig. 2C), TAT increased for both aquatic invertebrates (mainly because of pyrethroids; Fig. 2D) and terrestrial pollinators (mainly because of neonicotinoids; Fig. 2E) at the same rate observed for US agriculture as a whole (fig. S8, A and C). We verified that the toxicity per hectare of insecticides applied to *Bt* corn is equal to that for non-*Bt* corn (Fig. 2D, fig. S13, and fig. S14, C to F). The increasing insecticide TAT may be a result of preemptive, possibly unnecessary applications (4) or resistance (17). Our analysis suggests that

Fig. 2. Annual applied amount (i.e., mass) and nontarget species toxicity of the main classes of pesticides used in two of the most widely grown GM crops—soybeans and corn—in the US between 1992 and 2016.

(A) Amount of herbicides applied in soybeans (Mann-Kendall tests for monotonic trend: $\tau = 0.873$, $P < 0.001$). (B) TAT_{terr-plants} of 78 herbicides applied in soybeans ($\tau = 0.387$, $P = 0.129$). (C) Amount of insecticides applied in corn ($\tau = -0.553$, $P = 0.019$). (D) TAT_{aqua-inverts} of 72 insecticides applied in corn ($\tau = 0.5$, $P = 0.017$). (E) TAT_{pollinators} of 63 insecticides applied in corn ($\tau = 0.653$, $P = 0.009$). Lines in (A) and (C) were fitted using generalized additive models.



claims of reduced chemical insecticide use in US *Bt* crops (8, 9, 28) simply reflect the considerably lower application rates required for more recently developed, more toxic insecticide classes, whereas the TAT_{pollinators} and TAT_{aqua-inverts} both continue to increase.

TAT values may increase even more in global agriculture than they do in the US as important TAT drivers increase simultaneously. Such global developments include increased pesticide sales in Asia, Latin America, and Europe (9); expanded global cropland area (www.fao.org/faostat); and increased global pesticide use (29). Widespread resistance development (17), increasing field size (7), decreasing crop diversification (7), international market connectedness (30), and increasing temperatures (5) are key drivers of these developments. Although insecticide effects have been repeatedly documented (2, 15, 22), invertebrate biodiversity trends are generally debated (25, 26), and large-scale studies often do not focus on pesticides (25, 26, 31, 32). The unavailability of open-access pesticide use data in many regions, such as Latin America, the EU, China, and Russia, also prevents analyses such as those presented here, which potentially masks a crucial driver of the global biodiversity decline.

Despite being based on high-quality, curated data, our analysis carries some uncertainties.

The link between pesticide use and potential ecological impacts is formed by complex processes at different scales, and the methods applied here can only be indicative of the role pesticide use plays in the degradation of ecosystems, even at large scales. In light of the multiple emergent risks and resistance problems (6, 17), pesticide risks should be more integrated into policy strategies (33) to develop resilient global production systems (30, 31). Advancements in precision agriculture, mixed and organic farming, and nanoscale delivery platforms provide examples of how agriculture can develop productively while reducing environmental impacts (34, 35). Because 61% of US drinking water originates from surface waters, according to the EPA, TAT-based pesticide evaluations may also benefit human health evaluations. Overall, a system-centric view is conducive to understanding the dynamics of pesticide use on medium to large scales (36), and this is even more important given that ecosystem-wide pesticide impacts are becoming increasingly evident (2, 11, 12, 16).

REFERENCES AND NOTES

1. A. R. Kniss, *Nat. Commun.* **8**, 14865 (2017).
2. C. A. Hallmann, R. P. B. Foppen, C. A. M. van Turnhout, H. de Kroon, E. Jongejans, *Nature* **511**, 341–343 (2014).
3. S. Stehle, R. Schulz, *Proc. Natl. Acad. Sci. U.S.A.* **112**, 5750–5755 (2015).

4. M. R. Douglas, J. F. Tooker, *Environ. Sci. Technol.* **49**, 5088–5097 (2015).
5. J. A. Ewald *et al.*, *Glob. Change Biol.* **21**, 3931–3950 (2015).
6. C. Lamberth, S. Jeanmart, T. Luksch, A. Plant, *Science* **341**, 742–746 (2013).
7. A. E. Larsen, F. Noack, *Proc. Natl. Acad. Sci. U.S.A.* **114**, 5473–5478 (2017).
8. C. D. Osteen, J. Fernandez-Cornejo, *Pest Manag. Sci.* **69**, 1001–1025 (2013).
9. E. Stokstad, G. Grullón, *Science* **341**, 730–731 (2013).
10. See the supplementary materials.
11. D. A. Stanley *et al.*, *Nature* **528**, 548–550 (2015).
12. B. A. Woodcock *et al.*, *Science* **356**, 1393–1395 (2017).
13. M. R. Douglas, D. B. Sponsler, E. V. Lonsdorf, C. M. Grozinger, *Sci. Rep.* **10**, 797 (2020).
14. S. Fong, S. Louie, I. Werner, R. E. Connon, *San Franc. Estuary Watershed Sci.* **14**, 1–34 (2016).
15. H. A. Rogers *et al.*, *Environ. Sci. Technol.* **50**, 11974–11983 (2016).
16. I. Werner, T. M. Young, in *Encyclopedia of the Anthropocene*, D. A. Dellasala, M. I. Goldstein, Eds. (Elsevier, 2018), pp. 119–126.
17. F. Gould, Z. S. Brown, J. Kuzma, *Science* **360**, 728–732 (2018).
18. L. A. Morandin, M. L. Winston, *Ecol. Appl.* **15**, 871–881 (2005).
19. C. Stenoien *et al.*, *Insect Sci.* **25**, 528–541 (2018).
20. J. Wolfram, S. Stehle, S. Bub, L. L. Petschick, R. Schulz, *Environ. Sci. Technol.* **53**, 12071–12080 (2019).
21. J. Wolfram, S. Stehle, S. Bub, L. L. Petschick, R. Schulz, *Environ. Sci. Technol.* **52**, 14452–14460 (2018).
22. B. J. Mahler *et al.*, *Environ. Sci. Technol.* **54**, 5509–5519 (2020).
23. D. P. Weston *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **110**, 16532–16537 (2013).
24. J. C. Biesmeijer *et al.*, *Science* **313**, 351–354 (2006).
25. C. L. Outhwaite, R. D. Gregory, R. E. Chandler, B. Collen, N. J. B. Isaac, *Nat. Ecol. Evol.* **4**, 384–392 (2020).
26. S. Seibold *et al.*, *Nature* **574**, 671–674 (2019).
27. C. J. Vorosmarty *et al.*, *Nature* **467**, 555–561 (2010).
28. E. D. Perry, F. Ciliberto, D. A. Hennessy, G. Moschini, *Sci. Adv.* **2**, e1600850 (2016).
29. E. S. Bernhardt, E. J. Rosi, M. O. Gessner, *Front. Ecol. Environ.* **15**, 84–90 (2017).
30. M. Nyström *et al.*, *Nature* **575**, 98–108 (2019).
31. D. Tilman *et al.*, *Nature* **546**, 73–81 (2017).
32. R. van Klink *et al.*, *Science* **368**, 417–420 (2020).
33. P. Kudsik, L. N. Jørgensen, J. E. Ørum, *Land Use Policy* **70**, 384–393 (2018).
34. P. Mäder *et al.*, *Science* **296**, 1694–1697 (2002).
35. P. Vega-Vásquez, N. S. Mosier, J. Irudayaraj, *Front. Bioeng. Biotechnol.* **8**, 79 (2020).
36. C. J. Topping, A. Aldrich, P. Berry, *Science* **367**, 360–363 (2020).
37. R. Schulz, S. Bub, L. L. Petschick, S. Stehle, J. Wolfram, Applied pesticide toxicity shifts towards plants and invertebrates, even in GM crops, version v1, Zenodo (2021); <https://doi.org/10.5281/zenodo.4537036>.

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and have been supplemented for some species groups with data from www.efsa.europa.eu/en/data/chemical-hazards-data. The RTLs, the data for additional analysis regarding GM corn, and the code for this analysis can be found at <https://static.magic.eco/> TAT and are archived on Zenodo (37).

SUPPLEMENTARY MATERIALS

science.sciencemag.org/content/372/6537/81/suppl/DC1
Materials and Methods
Figs. S1 to S14
Tables S1 to S6

References (38–63)
MDAR Reproducibility Checklist

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A shifting burden

In 1962, Rachel Carson's *Silent Spring* was published, and the world was forced to take notice of the unintended impacts of pesticides on wildlife. Since then, there has been a perceived reduction in the amount of pesticides used and a shift in the kinds of pesticides available. Schulz *et al.* looked at the type, amount, and toxicity of pesticides applied over the last 25 years. They found that despite decreasing total amounts applied and decreased impacts on vertebrates, toxicity—in particular to insects and aquatic invertebrates—has increased substantially.

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